# BBB/NBS seminar (BMED380)

SCAN ME

Thursday, October 6, 14:30 at the BBB, Auditorium 4

## Membrane protein modifications in neurodegenerative disease

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Acetylation of protein N-termini (Nt-acetylation) is one of the most frequently occurring protein modifications. Over the recent years, several of its vital cellular and physiological functions have been demonstrated.

In our current work we connect N-terminal acetylation of membrane proteins to neurodegenerative disease. We attack this topic from two different angles: 1) from an N-terminal acetyltransferase (NAA60) and 2) from an Nt-acetylated protein ($\alpha$-Synuclein).

Our previous work demonstrated that NAA60 is unique among the N-terminal acetyl transferases for its localization and function on intracellular membranes. Now we show that loss-of-function NAA60 genetic variants are linked to a very specific type of neuropathology. By interdisciplinary collaborations, we present clinical features, neuroimaging, and genetic details of eight cases from five families with NAA60 variants. We demonstrate loss of function at the protein level, accompanying phenotypes in cells and zebrafish, besides suggest a possible disease pathway.

The Parkinson's disease-linked protein $\alpha$-Synuclein is a substrate of Nt-acetylation. The modification has been suggested to impact on disease-properties such as aggregation propensity and membrane binding capacity. This statement is however based solely on in vitro data. In our ongoing work we study these effects in a suitable Nt-acetylation knockout cell line to investigate properties of $\alpha$-Synuclein with and without its Nt-acetyl group.

Chairperson: Svein Isungset Støve <svein.stove@uib.no>, Dept. of Biomedicine